



ORIGINAL RESEARCH ARTICLE

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Selection of an optimal method for the preparation of dual loaded flavono polymeric nanoparticle using analytical hierarchy process

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ABSTRACT

In this study, analytical hierarchy process was used to select an optimal method for the preparation of dual loaded flavono polymeric nanoparticles. Analytical hierarchy process involves structuring multiple choice criteria into a hierarchy, assessing the relative importance of criteria, comparing alternatives for each criterion and determining an overall ranking of the alternatives. Hierarchy model was developed with the goal in the first level, 10 criteria in the second level and methods for the preparation of polymeric nanoparticles in the third level. To assess the relative importance of criteria, all criteria were compared with each other using Saaty's scale. To compare the methods, all the methods for the preparation of polymeric nanoparticles were compared with each other for each criterion using Saaty's scale, which leads to the formation of pair-wise comparison matrixes and consistency ratio was calculated for the each pair-wise comparison matrix. The study result showed that the consistency ratio of each pair-wise comparison matrix were well within acceptable limits. Of 10 criteria, reproducible results received the maximum overall priority weight followed by desirable size. Of 10 methods, nanoprecipitation method received the maximum overall priority weight followed by supercritical fluid technology. Analytical hierarchy process has identified reproducible results as criteria preference and nanoprecipitation as an optimal method for the preparation of dual loaded flavono polymeric nanoparticles. The study concludes that the analytical hierarchy process has played a vital role in selecting an optimal method for the preparation of dual loaded flavono polymeric nanoparticles.

Key Words: Analytical Hierarchy Process, Flavonoids, Polymeric Nanoparticles, Nanoprecipitation.

INTRODUCTION

Flavonoids are the group of polyphenolic compounds found extensively in fruits, vegetables, grains, roots, flowers, tea and wine. Flavonoids exhibit various pharmacological activities including hepatoprotective, wound healing, anti-inflammatory, anti-cancer, anti-bacterial and anti-diabetic (Middleton, 1998). However, poor aqueous solubility of flavonoids limits its clinical utility. Hence, we intend to overcome this limitation by fabricating polymeric nanoparticulate drug delivery system. However, polymeric nanoparticles can be prepared by various techniques including solvent evaporation (Hoa *et al.*, 2012), salting-out (Rao *et al.*, 2011), nanoprecipitation (Yordanov *et al.*, 2010), polymerization, dialysis (Liu *et al.*, 2007), nano spray drying (Elzoghby *et al.*, 2012), polycondensation, desolvation (Gülseren *et al.*, 2012), ionic gelation (Fan *et al.*, 2012) and supercritical fluid technology (Sekhon, 2010), but the selection of an optimal method was a real concern, as the selection of an unsuitable method may result in loss of time, material and financial resources (Moorthi *et al.*, 2013). Hence, we intended to apply Analytical Hierarchy Process (AHP) decision-making tool in the selection of an optimal method for the preparation of dual loaded flavono polymeric nanoparticles.

MATERIALS AND METHODS

Analytical Hierarchy Process

AHP is a multi-criteria decision-making tool, which was developed by Dr. Thomas L. Saaty in 1970s. AHP has been

effectively implemented in various field of science including marketing, finance, education, public policy, economics, medicine and sports to identify a suitable decision. AHP technique involves structuring multiple choice criteria into a hierarchy, assessing the relative importance of criteria, comparing alternatives for each criterion and determining an overall ranking of the alternatives (Saaty, 2008; Chauhan *et al.*, 2008; Kumar *et al.*, 2009).

Structuring multiple choice criteria into a hierarchy

As a first step to make a decision in an organized way, a hierarchy model was developed with three levels. The goal (i.e. selection of an optimal method for the preparation of dual loaded flavono polymeric nanoparticles) was placed in the first level. Ten criteria were placed in the second level. The criteria (table 1) were selected based on the most crucial process and issue in the preparation of polymeric nanoparticles. Methods for the preparation of polymeric nanoparticles were placed in the third level. The methods (table 2) were selected based on the available literatures.

Assessing the relative importance of criteria

To assess the relative importance of criteria, all criteria were compared with each other. During comparison, weights were allotted as per Saaty's scale (Table 3), which results in the formation of the pair-wise comparison matrix. Consistency ratio (CR) was calculated for the pair-wise comparison matrix as follows $[CR=CI/RI]$, where CI is consistency index and calculated as $CI = (\lambda_{max}-n)/(n-1)$ and RI is a random index (consistency index for the n row matrixes of randomly generated comparisons in pairs (table 4). Consistency ratio value < 0.1 is considered acceptable, which indicates that the weights allotted are reasonable.

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Table 1: Criteria for the selection of an optimal method for the preparation of polymeric nanoparticles.

Criteria Code	Description
C 01	Easy availability of instrument
C 02	Simple operating procedure
C 03	Parameter calibration
C 04	Operator's knowledge
C 05	Reproducible results
C 06	Easy availability of excipients
C 07	Desirable size
C 08	Scale-up
C 09	Maximum nanoparticle output
C 10	Less expensive

Table 2: Methods for the preparation of polymeric nanoparticles.

Methods	Code
Polymerization	M ₁
Polycondensation	M ₂
Solvent Evaporation	M ₃
Salting-out	M ₄
Nanoprecipitation	M ₅
Dialysis	M ₆
Nano Spray Drying	M ₇
Desolvation	M ₈
Ionic Gelation	M ₉
Supercritical Fluid Technology	M ₁₀

Table 3: Saaty's scale.

Importance	Weights	
	i^{th} Vs j^{th}	j^{th} Vs i^{th}
Equally important	1	1
Equally to moderately more important	2	1/2
Moderately more important	3	1/3
Moderately to strongly more important	4	1/4
Strongly more important	5	1/5
Strongly to very strongly more important	6	1/6
Very strongly more important	7	1/7
Very strongly to extremely more important	8	1/8
Extremely more important	9	1/9

Comparing alternatives for each criterion

To compare the methods, all the methods for the preparation of polymeric nanoparticles were compared with each other for each criterion. During comparison, weights were allotted as per Saaty's scale, which results in the formation of the pair-wise comparison matrix. Consistency ratio was calculated for each pair-wise comparison matrix as mentioned above. Consistency ratio value < 0.1 is considered acceptable, which indicates that the weights allotted are reasonable.

Determining an overall ranking

From the pair-wise comparison matrix, priority weights were calculated. To calculate the priority weights, the average of normalized column (ANC) method is used. In ANC the elements of each column are divided by the sum of the column and then the elements in each resulting row are added and this sum is divided by the number of elements in the row (n). This is a process of averaging

over the normalized columns. In mathematical form, the priority weights can be calculated as below and ranks were allotted based on overall priority weights.

$$w_i = \frac{1}{n} \sum_{j=1}^n \frac{a_{ij}}{\sum_i a_{ij}}, i, j = 1, 2, \dots, n$$

RESULTS AND DISCUSSION

Structuring multiple choice criteria into a hierarchy

A hierarchy model was developed with the goal in the first level, ten criteria in the second level and ten methods in the third level (figure 1).

Assessing the relative importance of criteria

All ten criteria were compared with each other using Saaty's scale, which results in the formation of the pair-wise comparison matrix (table 5). Pair-wise comparison begins with comparing the relative importance of two criteria. There are n x (n-1) judgments required to develop the set of pair-wise comparison matrix. The decision makers have to compare/judge each criteria using Saaty's scale. The judgements are decided on the basis of the decision makers' or users' experience and knowledge. For example, when making pair-wise comparisons, if criteria C 01 is strongly more important or essential than C 02, then C 01 = 5 and C 02 = 1/5. Consistency ratio was calculated and found to be less than 0.1, which indicates that the weights allotted were reasonable.

Comparing alternatives for each criterion

All ten methods were compared with each other for each criterion using Saaty's scale, which results in the formation of the pair-wise comparison matrices (table 6 to table 15). Pair-wise comparison begins with comparing the relative importance of two methods. There are n x (n-1) judgments required to develop the set of pair-wise comparison matrix. The decision makers have to compare/judge each method using Saaty's scale. The judgements are decided on the basis of the decision makers' or users' experience and knowledge. For example, when making pair-wise comparisons, if method M₁ is strongly more important or essential than M₂, then M₁ = 5 and M₂ = 1/5.

Determining overall ranking

From the pair-wise comparison matrix, priority weights were calculated and ranks were allotted based on overall priority weights. Priority weights and ranking of criteria preferences were summarized in table 16 and figure 2. Out of 10 criteria, reproducible results (C 05) received the maximum overall priority weights (0.1989) followed by desirable size (C 07; 0.1746) and easy availability of instruments (C 01; 0.1525). AHP decision-making tool has identified reproducible results as criteria preference for the preparation of dual loaded flavono polymeric nanoparticles. Priority weights and ranking of method were summarized in table 17, figure 3 and figure 4. Out of 10 methods, nanoprecipitation (M₅) received the maximum overall priority weights (0.2271) followed by supercritical fluid technology (M₁₀: 0.1411) and dialysis method (M₆: 0.1243). AHP decision-making tool has identified nanoprecipitation as an optimal method for the preparation of dual loaded flavono polymeric nanoparticles.

Table 4: Random index table.

n	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
RI	0,00	0,00	0,52	0,89	1,11	1,25	1,35	1,40	1,45	1,49	1,51	1,54	1,56	1,57	1,58

Table 5: Pair-wise comparison for criteria preferences.

Criteria	C01	C02	C03	C04	C05	C06	C07	C08	C09	C10
C01	1	3	3	3	1/3	3	1/2	3	3	3
C02	1/3	1	1/3	1/3	1/3	1/3	1/3	3	1/3	3
C03	1/3	3	1	3	1/3	3	1/2	3	3	3
C04	1/3	3	1/3	1	1/3	3	1/3	3	3	3
C05	3	3	3	3	1	3	1	3	3	3
C06	1/3	3	1/3	1/3	1/3	1	1/3	3	1/3	3
C07	2	3	2	3	1	3	1	3	3	3
C08	1/3	1/3	1/3	1/3	1/3	1/3	1/3	1	1/3	1/3
C09	1/3	3	1/3	1/3	1/3	3	1/3	3	1	3
C10	1/3	1/3	1/3	1/3	1/3	1/3	1/3	3	1/3	1

CI: 0.1479; CR: 0.0992; λ_{max} : 11.3308

Table 6: Pair-wise comparison for the criteria C01.

Methods	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10
M1	1	1	1/2	1/2	1/5	1/2	3	1/2	1/2	5
M2	1	1	1/3	1/2	1/5	1/2	3	1/2	1/2	5
M3	2	3	1	1/3	1/9	1/3	3	1/3	1/3	5
M4	2	2	3	1	1/3	3	5	1/2	3	5
M5	5	5	9	3	1	9	9	5	5	9
M6	2	2	3	1/3	1/9	1	3	1/3	1/3	5
M7	1/3	1/3	1/3	1/5	1/9	1/3	1	1/3	1/3	2
M8	2	2	3	2	1/5	3	3	1	2	5
M9	2	2	3	1/3	1/5	3	3	1/2	1	5
M10	1/5	1/5	1/5	1/5	1/9	1/5	1/2	1/5	1/5	1

CI: 0.1091; CR: 0.0732; λ_{max} : 10.9823

Table 7: Pair-wise comparison for the criteria C02.

Methods	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10
M1	1	1	1/3	1/3	1/9	1/3	1/3	1/3	1/3	1/3
M2	1	1	1/3	1/3	1/9	1/3	1/3	1/3	1/3	1/3
M3	3	3	1	1/3	1/9	1/3	1/3	1/2	1/3	1/2
M4	3	3	3	1	1/9	3	1/3	3	3	3
M5	9	9	9	9	1	7	7	7	7	7
M6	3	3	3	1/3	1/7	1	1	3	3	2
M7	3	3	3	3	1/7	1	1	3	3	1/2
M8	3	3	2	1/3	1/7	1/3	1/3	1	3	1/2
M9	3	3	3	1/3	1/7	1/3	1/3	1/3	1	1/3
M10	3	3	2	1/3	1/7	1/2	2	2	3	1

CI: 0.1373; CR: 0.0921; λ_{max} : 11.2354

Table 8: Pair-wise comparison for the criteria C03.

Methods	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10
M1	1	1	1/3	1/3	1/3	1	1/5	1/3	1/3	1/5
M2	1	1	1/3	1/3	1/5	1	1/5	1/3	1/3	1/5
M3	3	3	1	1/3	1/2	3	1/5	2	2	1/5
M4	3	3	3	1	1/2	3	1/5	2	1/2	1/5
M5	3	5	2	2	1	3	1/5	3	3	1/5
M6	1	1	1/3	1/3	1/3	1	1/5	1/3	1/3	1/5
M7	5	5	5	5	5	5	1	5	5	1/2
M8	3	3	1/2	1/2	1/3	3	1/5	1	2	1/5
M9	3	3	1/2	2	1/3	3	1/5	1/2	1	1/5
M10	5	5	5	5	5	5	2	5	5	1

CI: 0.1057; CR: 0.0709; λ_{max} : 10.9511

Table 9: Pair-wise comparison for the criteria C04.

Methods	M ₁	M ₂	M ₃	M ₄	M ₅	M ₆	M ₇	M ₈	M ₉	M ₁₀
M ₁	1	1	1/5	1/5	1/5	1/3	1	1/5	1/5	1
M ₂	1	1	1/5	1/5	1/5	1/3	1	1/5	1/5	1
M ₃	5	5	1	3	1	3	3	2	2	3
M ₄	5	5	1/3	1	1/3	3	3	3	3	3
M ₅	5	5	1	3	1	5	5	3	3	5
M ₆	3	3	1/3	1/3	1/5	1	2	1/5	1/5	2
M ₇	1	1	1/3	1/3	1/5	1/2	1	1/5	1/5	1
M ₈	5	5	1/2	1/3	1/3	5	5	1	1/2	3
M ₉	5	5	1/2	1/3	1/3	5	5	2	1	3
M ₁₀	1	1	1/3	1/3	1/5	1/2	1	1/3	1/3	1

CI: 0.0913; CR: 0.0613; λ_{max} :10.8214

Table 10: Pair-wise comparison for the criteria C05.

Methods	M ₁	M ₂	M ₃	M ₄	M ₅	M ₆	M ₇	M ₈	M ₉	M ₁₀
M ₁	1	1	1/5	1/5	1/5	1/7	1/3	1/3	1/3	1/5
M ₂	1	1	1/3	1/3	1/7	1/7	1/3	1/3	1/3	1/5
M ₃	5	3	1	1	1/3	1/5	1/3	1	3	1/3
M ₄	5	3	1	1	1/5	1/5	1/3	1/2	1/2	1/5
M ₅	5	7	3	5	1	1/3	3	3	3	1/3
M ₆	7	7	5	5	3	1	3	5	5	3
M ₇	3	3	3	3	1/3	1/3	1	3	3	1
M ₈	3	3	1	2	1/3	1/5	1/3	1	1/2	1/5
M ₉	3	3	1/3	2	1/3	1/5	1/3	2	1	1/5
M ₁₀	5	5	3	5	3	1/3	1	5	5	1

CI: 0.1027; CR: 0.0689; λ_{max} :10.9239

Table 11: Pair-wise comparison for the criteria C06.

Methods	M ₁	M ₂	M ₃	M ₄	M ₅	M ₆	M ₇	M ₈	M ₉	M ₁₀
M ₁	1	1	1/3	1/3	1/3	1	1/3	1/3	1/3	3
M ₂	1	1	1/3	1/3	1/3	1/3	1/3	1/3	1/3	3
M ₃	3	3	1	1	1	3	1/3	2	3	3
M ₄	3	3	1	1	1	3	1/3	2	3	3
M ₅	3	3	1	1	1	3	1	3	3	5
M ₆	1	3	1/3	1/3	1/3	1	1/3	1/3	1/3	3
M ₇	3	3	3	3	1	3	1	3	3	3
M ₈	3	3	1/2	1/2	1/3	3	1/3	1	2	3
M ₉	3	3	1/3	1/3	1/3	3	1/3	1/2	1	3
M ₁₀	1/3	1/3	1/3	1/3	1/5	1/3	1/3	1/3	1/3	1

CI: 0.0924; CR: 0.0620; λ_{max} :10.8320

Table 12: Pair-wise comparison for the criteria C07.

Methods	M ₁	M ₂	M ₃	M ₄	M ₅	M ₆	M ₇	M ₈	M ₉	M ₁₀
M ₁	1	1/2	1/3	1/3	1/7	1/5	1/5	1/3	1/3	1/5
M ₂	2	1	1/3	1/3	1/7	1/5	1/5	1/3	1/3	1/5
M ₃	3	3	1	3	1/5	1/5	1/5	3	3	1/5
M ₄	3	3	1/3	1	1/7	1/5	1/5	3	3	1/5
M ₅	7	7	5	7	1	3	3	7	7	3
M ₆	5	5	5	5	1/3	1	2	5	5	3
M ₇	5	5	5	5	1/3	1/2	1	5	5	1/3
M ₈	3	3	1/3	1/3	1/7	1/5	1/5	1	1/3	1/5
M ₉	3	3	1/3	1/3	1/7	1/5	1/5	3	1	1/5
M ₁₀	5	5	5	5	1/3	1/3	3	5	5	1

CI: 0.1426; CR: 0.0957; λ_{max} :11.2835

Table 13: Pair-wise comparison for the criteria C08.

Methods	M ₁	M ₂	M ₃	M ₄	M ₅	M ₆	M ₇	M ₈	M ₉	M ₁₀
M ₁	1	1	1/3	1/3	1/3	1/3	1/3	1/3	1/3	1/3
M ₂	1	1	1/3	1/3	1/3	1/3	1/3	1/3	1/3	1/3
M ₃	3	3	1	1	1/2	3	1/3	2	2	1/5
M ₄	3	3	1	1	1/3	2	1/3	2	2	1/5
M ₅	3	3	2	3	1	3	1/3	3	3	1/5
M ₆	3	3	1/3	1/2	1/3	1	1/3	1/3	1/3	1/5
M ₇	3	3	3	3	3	3	1	5	5	1/3
M ₈	3	3	1/2	1/2	1/3	3	1/5	1	1/2	1/5
M ₉	3	3	1/2	1/2	1/3	3	1/5	2	1	1/5
M ₁₀	3	3	5	5	5	5	3	5	5	1

CI: 0.1344; CR: 0.0902; λ_{max} :11.209

Table 14: Pair-wise comparison for the criteria C09.

Methods	M ₁	M ₂	M ₃	M ₄	M ₅	M ₆	M ₇	M ₈	M ₉	M ₁₀
M ₁	1	1	1/3	1/3	1/3	1/3	1/3	1/3	1/3	1/3
M ₂	1	1	1/3	1/3	1/3	1/3	1/3	1/3	1/3	1/3
M ₃	3	3	1	1/2	1/2	3	1/3	2	2	1/3
M ₄	3	3	2	1	1/2	3	1/3	2	1/2	1/3
M ₅	3	3	2	2	1	3	3	3	3	1/3
M ₆	3	3	1/3	1/3	1/3	1	1/3	1/3	1/3	1/5
M ₇	3	3	3	3	1/3	3	1	3	3	1/3
M ₈	3	3	1/2	1/2	1/3	3	1/3	1	1/2	1/3
M ₉	3	3	1/2	2	1/3	3	1/3	2	1	1/3
M ₁₀	3	3	3	3	3	5	3	3	3	1

CI: 0.1200; CR: 0.0805; λ_{\max} :11.0796

Table 15: Pair-wise comparison for the criteria C10.

Methods	M ₁	M ₂	M ₃	M ₄	M ₅	M ₆	M ₇	M ₈	M ₉	M ₁₀
M ₁	1	1	1/3	1/3	1/3	1/3	3	1/3	1/3	3
M ₂	1	1	1/3	1/3	1/3	3	3	1/3	1/3	3
M ₃	3	3	1	1/3	1/3	1	1	1/3	1/3	3
M ₄	3	3	3	1	1/2	3	3	1/2	2	3
M ₅	3	3	3	2	1	3	3	3	3	3
M ₆	3	1/3	1	1/3	1/3	1	2	1/3	1/3	3
M ₇	1/3	1/3	1	1/3	1/3	1/2	1	1/3	1/3	2
M ₈	3	3	3	2	1/3	3	3	1	1	3
M ₉	3	3	3	1/2	1/3	3	3	1	1	3
M ₁₀	1/3	1/3	1/3	1/3	1/3	1/3	1/2	1/3	1/3	1

CI: 0.1253; CR: 0.0841; λ_{\max} :11.1277

Table 16: Priority weights and ranking of criteria preferences.

Criteria	C 01	C 02	C 03	C 04	C 05	C 06	C 07	C 08	C 09	C 10
M ₁	0.0533	0.0240	0.0292	0.0285	0.0229	0.0474	0.0205	0.0338	0.0342	0.0557
M ₂	0.0524	0.0240	0.0279	0.0285	0.0235	0.0440	0.0234	0.0338	0.0342	0.0716
M ₃	0.0611	0.0368	0.0696	0.1875	0.0659	0.1362	0.0626	0.0830	0.0902	0.0796
M ₄	0.1299	0.1118	0.0785	0.1554	0.0469	0.1362	0.0488	0.0771	0.0905	0.1479
M ₅	0.3633	0.4290	0.1092	0.2328	0.1537	0.1637	0.2843	0.1206	0.1673	0.2173
M ₆	0.0718	0.0896	0.0292	0.0531	0.2803	0.0555	0.1927	0.0462	0.0465	0.0663
M ₇	0.0256	0.1055	0.2488	0.0336	0.1136	0.2083	0.1335	0.1863	0.1470	0.0432
M ₈	0.1299	0.0544	0.0604	0.1137	0.0513	0.0971	0.0312	0.0579	0.0657	0.1529
M ₉	0.0956	0.0452	0.0627	0.1302	0.0544	0.0810	0.0390	0.0660	0.0879	0.1329
M ₁₀	0.0172	0.0798	0.2845	0.0366	0.1875	0.0307	0.1640	0.2954	0.2365	0.0326
Overall Priority	0.1525	0.0488	0.1220	0.0954	0.1989	0.0611	0.1746	0.0313	0.0763	0.0391
Rank	3	8	4	5	1	7	2	10	6	9

Table 17: Priority weights and ranking of methods.

Criteria	M ₁	M ₂	M ₃	M ₄	M ₅	M ₆	M ₇	M ₈	M ₉	M ₁₀
C 01	0.0081	0.0080	0.0093	0.0198	0.0554	0.0109	0.0039	0.0198	0.0146	0.0026
C 02	0.0012	0.0012	0.0018	0.0055	0.0209	0.0044	0.0051	0.0027	0.0022	0.0039
C 03	0.0036	0.0034	0.0085	0.0096	0.0133	0.0036	0.0304	0.0074	0.0076	0.0347
C 04	0.0027	0.0027	0.0179	0.0148	0.0222	0.0051	0.0032	0.0108	0.0124	0.0035
C 05	0.0046	0.0047	0.0131	0.0093	0.0306	0.0558	0.0226	0.0102	0.0108	0.0373
C 06	0.0029	0.0027	0.0083	0.0083	0.0100	0.0034	0.0127	0.0059	0.0049	0.0019
C 07	0.0036	0.0041	0.0109	0.0085	0.0496	0.0336	0.0233	0.0054	0.0068	0.0286
C 08	0.0011	0.0011	0.0026	0.0024	0.0038	0.0014	0.0058	0.0018	0.0021	0.0092
C 09	0.0026	0.0026	0.0069	0.0069	0.0128	0.0035	0.0112	0.0050	0.0067	0.0180
C 10	0.0022	0.0028	0.0031	0.0058	0.0085	0.0026	0.0017	0.0060	0.0052	0.0013
Overall Priority	0.0325	0.0332	0.0824	0.0909	0.2271	0.1243	0.1200	0.0751	0.0734	0.1411
Rank	10	9	6	5	1	3	4	7	8	2

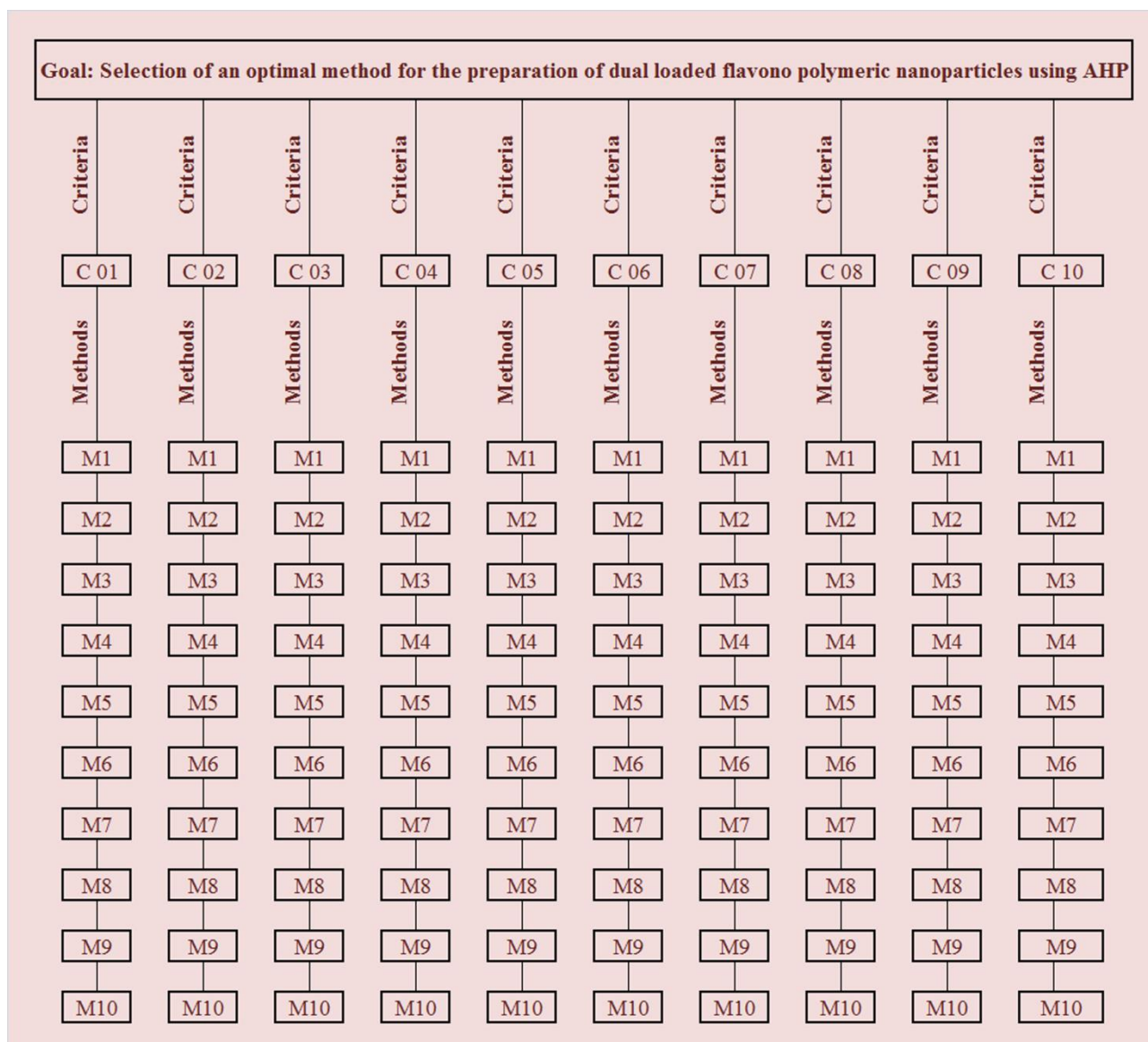


Figure 1: Hierarchy model for the selection of an optimal method for the preparation of dual loaded flavono polymeric nanoparticles using analytic hierarchy process.



Figure 2: Priority weights and ranking of criteria preferences.

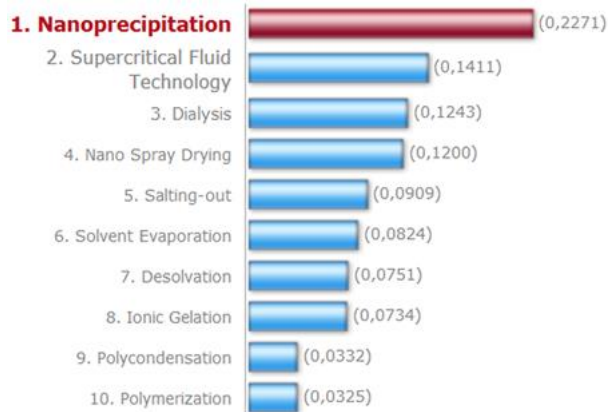


Figure 3: Priority weights and ranking of methods.

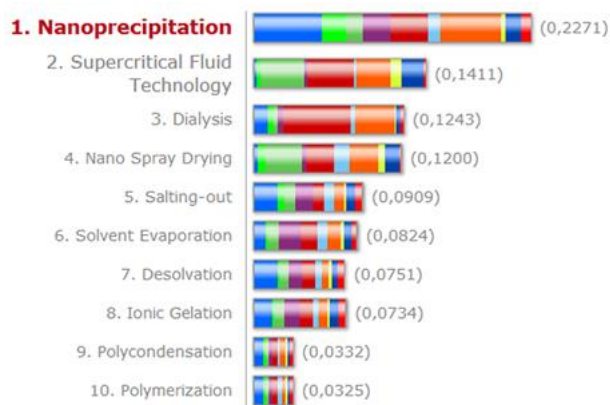


Figure 4: Priority weights and ranking of methods with criteria structure.

CONCLUSION

In the present study, we studied the problem of selecting an optimal method for the preparation of dual loaded flavono polymeric nanoparticles. Analytic hierarchy process decision-making tool was used to select an optimal method and the results suggested nanoprecipitation method would be an optimal method. The study concludes that the analytical hierarchy process has played a vital role in selecting an optimal method for the preparation of dual loaded flavono polymeric nanoparticles.

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